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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,763	07/08/2003	Ung-Kil Jee	T10086	9902

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/615,763	JEE, UNG-KIL	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *26-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed on 1/19/2007 have been fully considered but they are not persuasive.

Applicant's argue the motivation of the 35 U.S.C. 103 rejection over Lee et al. (U.S. Patent 6,743,436) in view of Chen et al. (U.S. Patent 6,383,471). Applicant's state that the Lee et al. reference is drawn to making an injectable composition and teaches away from making a composition that lacks a poloxamer. This argument is not found to be persuasive because Lee et al. teach that the composition comprises the poloxamer. Comprising language means that all of the elements can be present or some of the elements may be present. Therefore, the reference does not rely upon a poloxamer. Applicant's further argue that Chen et al. is directed to making an oral formulation and requires an ionizing agent and a surfactant for the therapeutic agent to be solubilized (Applicant's refer to Col. 1, lines 40-43 and Col. 31, lines 40-43). This argument is not found to be persuasive because the pharmaceutical compositions of the Chen et al. reference are comprised of the additional agents (see claim 1), meaning that the additional agents may or may not be present in the composition. Therefore, the reference does not rely on an ionizing agent in the composition. Applicant's further state that there is no mention in either reference to formulate a clear composition. Applicant's argue that there is no motivation to combine the references.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention

where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the purpose of the Lee et al. reference is to formulate an injectable propofol composition with an appropriate solvent and is free of the side effects listed in the Background section. Although the Chen et al. invention is described with reference to its value in oral dosage forms, it is stated that the invention is not so limited (Col. 4, lines 62-64) and can be formulated for parenteral administration (Col. 35, lines 9-13). Chen et al. teach pharmaceutical compositions that are capable of solubilizing therapeutically effective amounts of hydrophobic compounds. The Examiner agrees that neither reference refers to optical clarity (that deficiency is addressed in the second 35 U.S. 103 rejection); however, one would have been motivated to combine the two references to formulate an improved composition in which propofol would be solubilized.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant's argue that the 35 U.S.C. 103 rejection over Lee et al. and Chen et al. and in further view of De Tommaso (PG Pub 2002/0107291) teaches away from making the presently claimed invention and the motivation for combining the references is lacking. This argument is not found to be persuasive because De Tommaso states that "...a transparent injectable formulation of propofol may be obtained by mixing propofol with a bile acid and with a lecithin" (paragraph 0007). It is further taught in the same paragraph that the formulation is clear and the presence of foreign particles is controlled. Therefore, one of ordinary skill in the art would have been motivated to add a bile acid and lecithin to the present composition to formulate a clear and injectable formulation of propofol.

Applicant's remarks necessitated the following modified rejections.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 8-9, 13-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (U.S. Patent 6,743,436) in view of Chen et al. (U.S. Patent 6,383,471).

Lee et al. teach an injectable anesthetic composition comprised of 1 to 2% by weight of the total composition of propofol (meeting the limitations of 1 and 15; Col. 4,

lines 20-22). The composition further comprises a co-surfactant which is SOLUTOL HS 15 (polyethylene glycol 660 hydroxystearate, in an amount of 0.1 to 10% of the total composition (further meeting the limitation of claim 1 and 16; Col. 4, lines 36-38), egg lecithin in an amount of 0.1 to 5% of the total composition (meeting the limitations of claims 2-3, 8-9; Col. 4, line 38), ethanol and propylene glycol (meeting the limitations of claim 19; Col. 4, lines 36-48). A tonicity agent, such as glycerol is also added (meeting the limitation of claim 14; Col. 5, lines 38-40).

Lee et al. do not teach the injectable propofol composition further comprised of tetrahydrofurfuryl alcohol polyethyleneglycol ether, pH regulators, thickening agents, antioxidants, complexing agents, or antiseptics.

Chen et al. teach a pharmaceutical composition for the improved delivery of ionizable hydrophobic compounds (including propofol; Col. 7, line 11). The composition contains solubilizers to enhance the solubility of the active agent, with tetrahydrofurfuryl alcohol PEG ether, glycerol, and propylene glycol being among those preferred (further meeting the limitation of claim 1 and 17; Col. 31, lines 54-57 and Col. 32, line 46-48). The composition further contains pH regulators, such as ascorbic acid and gluconic acid (meeting the limitation of claims 18 and 20; Col. 11, lines 9-54), thickening agents such as methylcellulose (further meeting the limitation of claim 18 and 21; Col. 32, line 31), sulfates (further meeting the limitation of claim 18 and 23; Col. 33, line 21), benzyl alcohol (meeting the limitation of claim 24; Col. 31, line 45) and phosphate (as sodium phosphate; meeting the limitation of claim 22; Col. 11, line 30).

Accordingly, it would be obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Lee et al., which teach an anesthetic composition for intravenous injection comprised of propofol, polyethylene glycol 660 hydroxystearate, egg lecithin, ethanol, propylene glycol and glycerol, with Chen et al. which teaches utilizing the ingredients tetrahydrofurfuryl alcohol PEG ether, pH regulators, thickening agents, complexing agents, antioxidants, and antiseptics for improved delivery of ionizable hydrophobic compounds. One would have been motivated to combine the teachings of Lee et al. with Chen et al. in order to formulate an improved injectable composition, and with the addition of the tetrayhydrofurfuryl alcohol polyethylene glycol ether, provide a maximal concentration of propofol to be administered to a patient.

Claims 4-7, 10-12, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. and Chen et al. as applied to claims 1-3, 8-9, 13-24 above, and in further view of De Tommaso (PG Pub 2002/0107291).

Lee et al. and Chen et al. teach formulations comprised of propofol, polyethylene glycol 660 hydroxystearate, tetrahydrofurfuryl alcohol PEG ether, lecithin, a liquid excipient, a tonicity agent, pH regulators, thickening agents, complexing agents, antioxidants and antiseptics.

Lee et al. and Chen et al. do not teach formulations comprised of a bile salt or a mixture of a bile salt and lecithin.

De Tommaso also teaches an injectable pharmaceutical composition comprised of propofol, in which a bile salt, including glycocholic acid, cholic acid, and taurocholic acid, is incorporated into the injectable formulation (meeting the limitation of claims 4-7, 12; Pg. 1, paragraph 0015). The composition is further comprised of lecithin, and the formulation is prepared by adding lecithin to an aqueous solution of the bile salt (meeting the limitation of claims 10-11; Pg. 2, paragraph 0025, 0029).

It is obvious to vary and/or optimize the amount of bile salts provided in the composition, according to the guidance provided by De Tommaso to provide a composition having the desired properties such as the desired percentage weight of the bile salt for a more transparent injectable formulation. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Furthermore, it is obvious that because the components of the propofol composition of the prior art and the components of the present composition are the same, it is obvious that they will share the same physical properties, such as a transmittance at 660nm of greater than about 90%. Patent law states that "products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Accordingly, it would be obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Lee et al. and Chen which teach an anesthetic composition for intravenous injection comprised of propofol, polyethylene glycol 660 hydroxystearate, tetrahydrofurfuryl alcohol PEG ether, lecithin, a liquid excipient, a tonicity agent, pH regulators, thickening agents, complexing agents, antioxidants and antiseptics, with De Tommaso et al. which teach an injectable composition comprised of propofol and bile salts. One having ordinary skill in the art would be motivated to combine the teachings of Lee et al. and Chen et al. with De Tommaso to provide an injectable anesthetic composition that is transparent and clear and free of foreign particles inside the vial or bottle, which is important for product safety (as taught by De Tommaso, paragraph 0007).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER